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LUCAS & MERCANTI, LLP
475 PARK AVENUE SOUTH
15TH FLOOR
NEW YORK, NY 10016

EXAMINER	
NOGUEROLA, ALEXANDER STEPHAN	
ART UNIT	**PAPER NUMBER**
1753	

DATE MAILED: 08/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/083,845	ARMSTRONG, DANIEL	
	Examiner	Art Unit	
	ALEX NOGUEROLA	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-6,8-13,15,17 and 22-30* is/are pending in the application.

4a) Of the above claim(s) *18-21* is/are withdrawn from consideration.

5)☒ Claim(s) *27-29* is/are allowed.

6)☒ Claim(s) *1,3-6,8-13,15,17,22-26 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Rejections and Objections pending since the Office action of March 20, 2006

1. All previous objections and rejections are withdrawn.

Response to Arguments

2. Applicant's arguments with respect to the pending claims have been considered but are moot in view of the new grounds of rejection. It will be noted with regard to the rejections of claim 26 based on Fuhr that Fuhr discloses isoelectric focusing in a capillary, that is capillary isoelectric focusing. Whatever alleged differences exist between Applicant's isoelectric focusing and Fuhr's, such as those discussed by Applicant on pages 19-20 of his Amendment of June 19, 2006, are moot unless they are set forth in the claims.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 3, 4, 5, and 22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Claim 1 requires "separating said one or more microbes/cells in said moving fluid by means of electrophoresis *so as to focus* said one or more microbes/cells in said moving fluid and to separate one from another [emphasis added]". The word "focus" and its derivatives such as "focusing" only occurs in the original disclosure in the context of isoelectric focusing, which Applicant is disclaiming since he has removed it from the claim by amendment. Furthermore, Applicant argues that the polymer focuses the microbes/cells: "The innovative use of the diluted neutral polymers in the running buffer focuses the microbes/cells into a compact zone. This obvious focusing effect can be seen in the electropherograms as very sharp peaks." See page 17 of the Amendment of June 19, 2006. Thus, to focus the microbes/cells in moving fluid by electrophoresis is new matter.

5. Claims 1, 3, 4, 5, 6, 8-13, 15, 17, 22, 23, 24, and 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Claim 1 requires the moving fluid to comprise "a dilute water soluble *neutral* polymer that *focuses* said microbes in said passageway during said separating step [emphasis added]." Independent claims 6,10, and 15 also require a neutral water-soluble polymer. The word "focus" and its derivatives such as "focusing" only occurs in the original disclosure in the context of isoelectric focusing, which Applicant is disclaiming since he as removed it from the claim by amendment. Also, in the original disclosure any discussion of polymer in the running buffer mentions only its benefit to separation, not focusing. See for example, the bottom paragraphs on pages 14 and 24 of the specification. Although Applicant argues that the polymer focuses the microbes/cells: "The innovative use of the diluted neutral polymers in the running buffer focuses the microbes/cells into a compact zone. This obvious focusing effect can be seen in the electropherograms as very sharp peaks," (See page 17 of the Amendment of June 19, 2006) there is no showing that the polymer focuses the microbes/cells. For example, there is no graph showing narrower peaks with polymer compared without polymer during an electrophoresis run, other conditions being the same. Also, there is no mention of "neutral polymer" in the original specification. Some of the polymers

claimed to be neutral appear to actually be charged. See for example claim 22 and in U.S. Patent No. 7,033,474 B1 col. 18:33-38 and U.S. Patent No. 6,558,945 B1 col. 4:33-43.

6. Claim 30 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Although claim 30 has been amended by removing "isoelectric focusing" from the claim it implicitly still requires performing isoelectric focusing on sample in a moving fluid because it has the limitation of "separating said one or more microbes/cells in said moving fluid by means for electrophoresis so as to focus said one or more microbes/cells in said moving fluid" and all references to "focus" and its derivates such as "focusing" in the specification are only in regard to isoelectric focusing. Isoelectric focusing in a moving fluid is not supported in the original disclosure because Applicant's specification only discloses conventional isoelectric focusing: "The capillary isoelectric focusing is conducted in a conventional manner using conventional equipment." See Applicant's specification, page 15, third paragraph. Conventional isoelectric focusing does not involve moving fluid while focusing the sample, although the fluid may be moved *after* the sample components have been focused (mobilization).

See, for example, the first and second paragraphs in section 1.10 *Coated capillaries and salt mobilization. Background* on page 173 of Liu et al. "Review: Capillary isoelectric focusing as a tool in the examination of antibodies, peptides and proteins of pharmaceutical interest. Applicant's specification actually teaches away from moving fluid while focusing the sample components: "Samples were injected into the tube ... followed by a second injection of ampholyte for 129 seconds. *After focusing* for 5 min (voltage 20kV) samples were *mobilized with low pressure* (0.5psi) rinse while the 20 kV voltage was maintained [emphasis added]." See first full paragraph on page 28. Thus, there is no support in the original disclosure for moving fluid during isoelectric focusing. Also, the reference provided by Applicant with his Amendment of June 19, 2006 states, "The EOF needs to be eliminate in cIEF as the flow would flush the ampholytes from the capillary before focusing was complete."

7. Note that dependent claims will have the deficiencies of base and intervening claims.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 1, 3, 4, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ebersole et al. (US 5,578,460) ("Ebersole") in view of Johnson et al. (EP 077325 A2) ("Johnson"), the CAPLUS abstract of Barkas et al. ("Use of polyacrylamide gel electrophoresis for the preparation of oriented virus particle preparations," Doklady Akademii Nauk SSR (1979), 245(3), 736-9 (Biochem.) ("Barkas"), Silman (US 4,526,865) ("Silman"), Catsimpoolas (US 4,375,401)

("Catsimpoolas'), the CAPLUS abstract of Jenkins et al. ('Capillary isoelectric focusing of hemoglobin variants in the clinical laboratory," Clinica Chimica Acta (1999), 289(1-2), 121-132) ("Jenkins"), Grant et al. (GB 2348504 A) ("Grant"), .and Van Alstine (US 5,108,568).

Addressing claim 1, Ebersole discloses a process for separating and identifying intact microbes while maintaining the microbes intact comprising:

(a) obtaining sample comprising one or more intact microbes/cells from a substrate containing the microbes/cells (col. 21:5-36);

(b) introducing the sample into a passageway having a moving fluid therein (col. 6:24-27; col. 22:39-40; Figures 5b and 5c; col. 6:24-35; and col. 6:59-65);

(c) separating the one or more microbes/cells the moving fluid by means of capillary electrophoresis so as cause the one or more microbes/cells to move in the fluid and to separate one from another and from other components in said sample while maintaining the microbes/cells intact (col. 6:27-29; col. 22:47-50; col. 22:63-65); and

(d) analyzing the separated intact microbes/cells so as identify the microbes/cells (col. 6:35-47; col. 6:66 – col. 7:16; col. 22:32-38; and col. 23:2-11).

Although Ebersole discloses adding polymer to the running buffer to modify the viscosity (col. 15:2-5) or to the inner capillary wall (col. 14:43-47) to reduce electroendosmosis, Ebersole does not disclose adding a dilute neutral water soluble polymer that focuses the microbes in the passageway during the separating step. However, at the time of the invention it was known to use a gel while electrophoresising microbes/cells. See Barkas and the abstracts of Silman and Catsimpoolas. At the time

of the invention it was also known to add to an electrophoresis capillary a dilute water-soluble polymer that focuses biomolecules or cells in the passageway during the separating step. See, for example, col. 3:34 – col. 4:11 in Johnson; Jenkins (who uses methyl cellulose to separate red blood cells in a capillary), and the abstract; col. 3:9-15; in Grant the abstract; second full paragraph on page 18 and Example 9, which begins on page 30; and col.9:2-11 in Van Alstine (who discloses using polyethylene glycol to separate macromolecules, particles, or cells in a capillary). Thus, whether a separation medium is used, such as gel or neutral water-soluble polymer while separating the microbes/cells, barring a showing to the contrary, such as unexpected results, is just a matter of optimizing the separation of the microbes/cells as this was a known purpose for using gels or uncrosslinked polymer solution during electrophoresis. Whether the water-soluble polymer is "dilute" is just a matter of optimizing the sieving effect of the polymer.

Addressing claim 3, for the additional limitation of this claim see Figures 5a-5c in Ebersole.

Addressing claim 4, for the additional limitation of this claim see col. 15:38-55 in Ebersole

Addressing claim 22, for the additional limitation of this claim note that Johnson discloses at least hydroxyethylcelluslose. See col. 6:25-29. The other listed polymers were also used as electrophoresis separation media at the time of the invention. See, for example, Jenkins (who uses methyl cellulose to separate red blood cells in a capillary), and the abstract; col. 3:9-15; in Grant the abstract; second full paragraph on page 18 and Example 9, which begins on page 30; and col.9:2-11 in Van Alstine (who discloses using polyethylene glycol to separate macromolecules, particles, or cells in a capillary). It was within the skill of one with ordinary skill in the art at the time of the invention to select the optimum separation polymer from known separation polymers.

11. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ebersole et al. (US 5,578,460) ("Ebersole") in view of Johnson et al. (EP 077325 A2) ("Johnson"), Barkas et al. ("Use of polyacrylamide gel electrophoresis for the preparation of oriented virus particle preparations," Doklady Akademii Nauk SSR (1979), 245(3), 736-9 (Biochem.) ("Barkas"), Silman (US 4,526,865) ("Silman"), Catsimpoolas (US 4,375,401) ("Catsimpoolas'), the CAPLUS abstract of Jenkins et al. ('Capillary isoelecric focusing of hemoglobin variants in the clinical laboratory," Clinica Chimica Acta (1999), 289(1-2), 121-132) ("Jenkins"), Grant et al. (GB 2348504 A) ("Grant"), .and Van Alstine (US 5,108,568) as applied to claims 1-4 and 22 above, and further in view of the first page of "Streptococcus pyogenes" article downloaded from

www.textbookofbacteriology.net/streptococcus.html ("Streptococcus pyogenes") and "The Bacteria Antibotics Can't Kill" downloaded from www.tigr.org/~btran/ENTEROCCUS.html ("Enterococcus faecalis").

Ebersole does not mention an animal substrate; however, it would have been obvious to one with ordinary skill in the art at the time the invention was made to use an animal substrate because Ebersole discloses the microbes streptococcus pyogenes and enterococcus faecalis, which cause infections in humans. See "streptococcus pyogenes" and "enterococcus faecalis"

12. Claims 6, 8-13, and 22-24 are rejected under 35 U.S.C. 103(a) as being obvious by Durr et al. (US 5,723,031) ("Durr") in view of Johnson et al. (EP 077325 A2) ("Johnson"), the CAPLUS abstract of Barkas et al. ("Use of polyacrylamide gel electrophoresis for the preparation of oriented virus particle preparations," Doklady Akademii Nauk SSR (1979), 245(3), 736-9 (Biochem.) ("Barkas"), Silman (US 4,526,865) ("Silman"), and Catsimpoolas (US 4,375,401) ("Catsimpoolas"), the CAPLUS abstract of Jenkins et al. ('Capillary isoelecric focusing of hemoglobin variants in the clinical laboratory," Clinica Chimica Acta (1999), 289(1-2), 121-132) ("Jenkins"), Grant et al. (GB 2348504 A) ("Grant"), .and Van Alstine (US 5,108,568).

Addressing claim 6, Durr discloses a process for diagnosing disease caused by microbes (see in Applicant's specification page 9, first sentence of the fourth full paragraph: "Microbes such as bacteria, viruses and fungi ... [emphasis added]") comprising:

(a) obtaining a sample comprising one or more intact microbes/cells from a substrate containing the microbes (Table 1 in column 5);

(b) introducing the sample into a passageway having a fluid therein (col. 4:31-36 and Table 2 – Injection in column 5);

(c) separating the one or more microbes the fluid by means of capillary electrophoresis so as to cause the one or more microbes to move in the fluid and to separate one from another and from other components in said sample while maintaining the microbes intact (col. 4:39-40; col. 5:24-27; claim 1 preamble; col. 10:36-57; and Figures 11(a) and (b)); and

(d) analyzing the separated intact microbes so as identify the microbes (col. 4:40-50 and col. 5:35-41).

Durr does not mention (i) obtaining the sample from an organism stricken with a disease caused by the microbes, (ii) associating the microbe with a disease so as to diagnose the disease, (iii) and using in the fluid a dilute water soluble polymer that focuses the microbes in the passageway during the separating step.

As for obtaining the sample from an organism stricken with a disease caused by the microbes, although not mentioned by Durr it would have been obvious to do so because Durr states, 'The viruses can be identified directly from any sample matrix, for

example, from biological material (serum, urine, cells, plasma, cell supernatant, aqueous humour, saliva, et cetera) ..." (col. 2:52-59) and exemplifies the invention by separating and identifying active foot-and-mouth virus (col. 6:21-61).

As for associating the microbe with a disease so as to diagnose the disease it is clear from the just cited portions of Durr that Durr intended his invention to be used in real –world settings to, for example, identify from a bodily fluid whether an ill person has foot-and-mouth disease.

As for using in the fluid a dilute neutral water-soluble polymer that focuses the microbes in the passageway during the separating step, at the time of the invention it was known to use a gel while electrophoresising microbes/cells. See Barkas and the abstracts of Silman and Catsimpoolas. At the time of the invention it was also known to add to an electrophoresis capillary a dilute water-soluble polymer that focuses biomolecules or cells in the passageway during the separating step. See, for example, col. 3:34 – col. 4:11 in Johnson, in Grant the abstract; second full paragraph on page 18 and Example 9, which begins on page 30; Jenkins (who uses methyl cellulose to separate red blood cells in a capillary), and the abstract; col. 3:9-15, and col.9:2-11 in Van Alstine (who discloses using polyethylene glycol to separate macromolecules, particles, or cells in a capillary). Thus, whether a separation medium is used, such as gel or neutral water-soluble polymer while separating the microbes/cells, barring a showing to the contrary, such as unexpected results, is just a matter of optimizing the separation of the microbes/cells as this was a known purpose for using gels or

uncrosslinked polymer solution during electrophoresis. Whether the water-soluble polymer is "dilute" is just a matter of optimizing the sieving effect of the polymer.

Addressing claims 8 and 13, for the additional limitations of these claims see Durr col. 4:31-61.

Addressing claims 9 and 12, Durr states, 'The viruses can be identified directly from any sample matrix, for example, from biological material (serum, urine, cells, plasma, cell supernatant, aqueous humour, saliva, et cetera) or from non-biological formulations (water, medicaments, soil samples, et cetera) (col. 2:52-59) and exemplifies the invention by separating and identifying active foot-and-mouth virus (col. 6:21-61), which infects animals and people.

Addressing claim 10, Durr discloses a process for determining the binding affinity (col. 10:36-38) of a drug/other substance with a microbe/cell (see in Applicant's specification page 9, first sentence of the fourth full paragraph: "Microbes such as bacteria, viruses and fungi ... [emphasis added]") comprising

(a) obtaining a sample comprising one or more intact microbes/cells from a substrate containing the microbes/cells (col. 2:52-59);

(b) combining the sample with a drug or other substance in a fluid media to form a suspension and to allow the microbe/cell to bind with the drug/other substance (col. 10:45-47 and col. 11:3-6);

(c) introducing the suspension into a passageway having a fluid therein (col. 10:46-49 and col. 11:6-7);

(d) subjecting the suspension to capillary electrophoresis so as to cause the microbes/cells, and drug/other substance and bound microbes/cells-drug/other substance to move in the fluid and to separate from one another while maintaining the microbes/cells, the drug/other substance and the bound microbes/cells-drug/other substance intact (claim 1 preamble; col. 10:45-57; and col. 11:6-21); and

(e) analyze the separated, intact bound microbes/cells-drug/other substance to determine their affinity for each other (col. 10:45-67; col. 11:16-19; and col. 12:16-21).

As for using in the fluid a dilute neutral water-soluble polymer that focuses the microbes in the passageway during the separating step, at the time of the invention it was known to use a gel while electrophoresising microbes/cells. See Barkas and the abstracts of Silman and Catsimpoolas. At the time of the invention it was also known to

add to an electrophoresis capillary a dilute water-soluble polymer that focuses biomolecules or cells in the passageway during the separating step. See, for example, col. 3:34 – col. 4:11 in Johnson; in Grant the abstract; second full paragraph on page 18 and Example 9, which begins on page 30; the Jenkins abstract (who uses methyl cellulose to separate red blood cells in a capillary); and the abstract; col. 3:9-15, and col.9:2-11 in Van Alstine (who discloses using polyethylene glycol to separate macromolecules, particles, or cells in a capillary). Thus, whether a separation medium is used, such as gel or neutral water-soluble polymer while separating the microbes/cells, barring a showing to the contrary, such as unexpected results, is just a matter of optimizing the separation of the microbes/cells as this was a known purpose for using gels or uncrosslinked polymer solution during electrophoresis. Whether the water-soluble polymer is "dilute" is just a matter of optimizing the sieving effect of the polymer.

Addressing claim 11, for the additional limitation of this claim see Durr col. 10:36-49 and col. 10:59-62.

Addressing claims 22-24, for the additional limitations of these claims note that Johnson discloses at least hydroxyethylcelluslose. See col. 6:25-29. The other listed polymers were also used as electrophoresis separation media at the time of the invention. See, for example, Jenkins (who uses methyl cellulose to separate red blood

cells in a capillary), and the abstract; col. 3:9-15; in Grant the abstract; second full paragraph on page 18 and Example 9, which begins on page 30; and col.9:2-11 in Van Alstine (who discloses using polyethylene glycol to separate macromolecules, particles, or cells in a capillary). It was within the skill of one with ordinary skill in the art at the time of the invention to select the optimum separation polymer from known separation polymers.

13. Claims 15-17 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over McCormick et al. (US 6,613,211 B1) ("McCormick") in view of Johnson et al. (EP 077325 A2) ("Johnson") and Grant et al. (GB 2348504 A) ("Grant") the CAPLUS abstract of Jenkins et al. ('Capillary isoelecric focusing of hemoglobin variants in the clinical laboratory," Clinica Chimica Acta (1999), 289(1-2), 121-132) ("Jenkins"), and Van Alstine (US 5,108,568).

Addressing claim 15, McCormick discloses a process for determining the viability of microbes/cells comprising

(a) obtaining a sample containing one or more intact microbes/cells from a substrate containing the microbes or cells (col. 12:38-40);

(b) dyeing the sample with a dye that causes viable microbes/cells to be distinguished from non-viable micros/cells (col. 12:47-49 and col. 11:10-16); and

(c) introducing the dyed sample into a passageway having a fluid therein (col. 11:26-27);

(d) separating the one or more microbes/cells in the fluid by means of an capillary electrophoresis so as to cause the one or more microbes to move in the fluid and to separate one from another and from other components in said sample while maintaining the microbes intact (implied by col. 11:53-55 and col. 13:26-30, which discloses applying EOF (electrosmotive force) and voltage differentials to the channel, which are of capillary dimensions (col. 13:1-14). Note that although not stated, barring a contrary showing, separation will inherently occur among fluid components that have different electrophoretic motilities).

McCormick does not specifically mention analyzing the separated intact microbes/cells so as to identify viable microbes/cells from non-viable microbes/cells based on the dye. However, it would have been obvious to one with ordinary skill in the art at the time the invention was made to do so because McCormick teaches determining cellular response to toxic agents by using vital dyes to mark cells killed by the toxic agents. See col. 12:36-49.

McCormick does not disclose adding a dilute water soluble polymer that focuses the microbes in the passageway during the separating step, although it should be noted that McCormick discloses adding a water soluble polymer as a coating the capillary walls to modify any electrosomotic force that may occur during electrophoresis. See col. 5:1-12.

At the time of the invention it was known to add to an electrophoresis capillary a dilute water-soluble polymer that focuses biomolecules in the passageway during the separating step. See, for example, col. 3:34 – col. 4:11 in Johnson. More especially, it was known at the time of the invention to add a dilute water-soluble polymer that focuses microbes in the passageway during the separating step. See in Grant the abstract; second full paragraph on page 18 and Example 9, which begins on page 30. It would have been obvious to one with ordinary skill in the art at the time of the invention to add a dilute water soluble polymer as taught by Grant or Van Alstine or Jenkins in the invention of McCormick because it was known that dilute water soluble polymers can enhance separation of large biomolecules and so would be expected to enhance separation of microbes and because more especially, as shown by Grant, the separation of the microbes from each other can be optimized (Figures 13 and 14). Whether the water-soluble polymer is "dilute" is just a matter of optimizing the sieving effect of the polymer.

Addressing claim 17, for the limitation of this claim see McCormick Figures 1-3 and col. 13:1-16.

Addressing claim 25, for the additional limitation of this claim note that Johnson discloses at least hydroxyethylcelluslose. See col. 6:25-29. The other listed polymers were also used as electrophoresis separation media at the time of the invention. See, for example, Jenkins (who uses methyl cellulose to separate red blood cells in a capillary), and the abstract; col. 3:9-15; in Grant the abstract; second full paragraph on page 18 and Example 9, which begins on page 30; and col.9:2-11 in Van Alstine (who discloses using polyethylene glycol to separate macromolecules, particles, or cells in a capillary). It was within the skill of one with ordinary skill in the art at the time of the invention to select the optimum separation polymer from known separation polymers.

14. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fuhr et al. (US 6,833,061 ("Fuhr").

Addressing claim 26, Fuhr discloses a process for separating and identifying intact particles while maintaining the particles intact comprising

(a) obtaining a sample comprising one or more intact particles (implied since a sample is separated);

(b) introducing the sample into a passageway having a fluid therein (col. 6:7-34);

(c) separating the one or more particles in the fluid by capillary isoelectric focusing so as to cause the one or more micros/cells to move in the fluid and to separate from one another and from any other components in the sample while maintaining the particles intact (Figure 1; col. 5:8-9 and col. 6:35 – col. 7:5); and

(d) analyzing the separated intact particles so as to identify the particles (col. 7:1-5 and col. 8:59-67),

wherein the fluid comprises an ampholyte that focuses the microbes in the passageway during the separating step (col. 6:3-6; col. 4:16-37).

While Fuhr does not have an example in which the particles are intact microbes or cells it would have been obvious to one with ordinary skill to use his method to isoelectrically separate microbes or cells because Fuhr clearly contemplates such a use:

> Isoelectric separation according to the invention can be implemented with ampholytic molecules or all other synthetic or biological particles (especially cells or viruses) that exhibit electrical characteristics like those of ampholytic molecules, in particular a net charge or charge density that is a pH function of the surroundings [emphasis added]. *See col. 4:16-21.*

> The method according to claim 1, wherein the particles to be separated comprise ampholytic molecules or other particles, synthetic particles or biological cells, viruses, or other biological objects whose exhibit electrical characteristics correspond to the electrical characteristics of ampholytic molecules [emphasis added]. *Claim 2.*

15. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fuhr et al. (US 6,833,061 ("Fuhr") in view of Johnson et al. (EP 077325 A2) ("Johnson") and Grant et al. (GB 2348504 A) ("Grant") the CAPLUS abstract of Jenkins et al. ('Capillary isoelecric focusing of hemoglobin variants in the clinical laboratory," Clinica Chimica Acta (1999), 289(1-2), 121-132) ("Jenkins"), and Van Alstine (US 5,108,568).

Addressing claim 30, Fuhr discloses a process for separating and identifying intact microbes while maintaining the microbes intact comprising

(a) obtaining a sample comprising one or more intact particles (implied since a sample is separated);

(b) introducing the sample into a passageway having a moving fluid therein (col. 1:8-13 and col. 6:7-34 – note guiding fluid);

(c) separating (by isoelectric focusing) the one or more particles in the moving fluid by means of an electric field so as to focus the one or more particles in the moving fluid and to separate one from another and form any other components in the sample while maintaining the particles intact (Figure 1; col. 5:8-9; and col. 6:35 – col. 7:5); and

analyzing the separated intact particles so as to identify the particles (col. 7:1-5 and col. 8:59-67),

wherein the moving fluid comprises an ampholyte that focuses the microbes/cells in the passageway during the isoelectric focusing step (col. 1:8-13; col. 6:3-6; and col. 4:16-37).

While Fuhr does not have an example in which the particles are intact microbes or cells it would have been obvious to one with ordinary skill to use his method to

isoelectrically separate microbes or cells because Fuhr clearly contemplates such a use:

> Isoelectric separation according to the invention can be implemented with ampholytic molecules or all other synthetic or biological particles (especially cells or viruses) that exhibit electrical characteristics like those of ampholytic molecules, in particular a net charge or charge density that is a pH function of the surroundings [emphasis added]. *See col. 4:16-21.*

> The method according to claim 1, wherein the particles to be separated comprise ampholytic molecules or other particles, synthetic particles or biological cells, viruses, or other biological objects whose exhibit electrical characteristics correspond to the electrical characteristics of ampholytic molecules [emphasis added]. *Claim 2.*

> The invention concerns methods and devices for isoelectric separation of particles whose charge characteristics depend on the pH value of a guiding fluid, especially for separating ampholytic suspended particles, colloids or biological cells. The invention concerns in particular the separation of such particles from a guiding fluid flow. [emphasis added] *See col. 1:8-13.*

Fuhr does not disclose adding a dilute water soluble polymer that focuses the microbes in the passageway during the separating step. At the time of the invention it was known to add to an electrophoresis capillary a dilute water-soluble polymer that focuses biomolecules in the passageway during the separating step. See, for example, col. 3:34 – col. 4:11 in Johnson. More especially, it was known at the time of the invention to add a dilute water-soluble polymer that focuses microbes in the passageway during the separating step. See in Grant the abstract; second full

paragraph on page 18 and Example 9, which begins on page 30. It would have been obvious to one with ordinary skill in the art at the time of the invention to add a dilute water soluble polymer as taught by Grant or Van Alstine or Jenkins in the invention of Fuhr because it was known that dilute water soluble polymers can enhance separation of large biomolecules and so would be expected to enhance separation of microbes and because more especially, as shown by Grant, the separation of the microbes from each other can be optimized (Figures 13 and 14). Whether the water-soluble polymer is "dilute" is just a matter of optimizing the sieving effect of the polymer.

Allowable Subject Matter

16. Claims 27-29 are allowed.

17. The following is a statement of reasons for the indication of allowable subject matter:

a) Claim 27; the combination of limitations requires "obtaining a sample containing one or more intact microbes from an organism stricken with a disease caused by said microbe" and "associating said microbe with a disease so as to diagnose said disease." Fuhr does not mention any sources for the microbes nor diagnosing a disease.

b) Claim 28; the combination of limitations requires "combining the sample with a drug or other substance in a fluid media to form a suspension and to allow said microbe/cell to bind with said drug/other substance." Fuhr does not disclose binding the microbe/cell to a drug/other substance. Fuhr arguably teaches away from such a step since his method is a purification method. See col. 2:31-46.

c) Claim 29; the combination of limitations requires "dying said sample with a dye that causes viable microbes/cells to be distinguished from non-viable microbes/cells." Fuhr does not disclose dying the microbes/cell. Fuhr arguably teaches away from such a step since his method is a purification method. See col. 2:31-46.

Final Rejection

18. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEX NOGUEROLA whose telephone number is (571) 272-1343. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NAM NGUYEN can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Alex Noguerola
Primary Examiner
AU 1753
August 22, 2006